EO/US
PCT/EP98/06056

PA ENT COOPERATION TREAT Y

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing: 21 October 1999 (21.10.99)	
International application No.: PCT/EP98/06056	Applicant's or agent's file reference: 44.68617/000
International filing date: 24 September 1998 (24.09.98)	Priority date: 26 September 1997 (26.09.97)
Applicant: AIDAM, Elke et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International preliminary Examining Authority on:

   05 March 1999 (05.03.99)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was
   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland** Facsimile No.: (41-22) 740.14.35	Authorized officer: J. Zahra Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

FRANK B. DEHN & CO.
Attn. Cockbain, J.
179 Queen Victoria Street
London EC4V 4EL
UNITED KINGDOM

FILE 68617/000
18 JAN 1999
RECEIVED
Ro 26/1/99 DXM
ANSD

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

	Date of mailing (day/month/year) 13/01/1999
Applicant's or agent's file reference 44.68617/000	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/EP 98/06056	International filing date (day/month/year) 24/09/1998
Applicant HELISPIN POLARISIERTE GASE GMBH et al.	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicants's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

DUE DATE(S) NOTED
13/3/99

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Carl Hakim

Form PCT/ISA/220 (January 1994)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international pbulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]: "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]: "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREA[TY]

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 44.68617/000	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 98/ 06056	International filing date *(day/month/year)* 24/09/1998	(Earliest) Priority Date *(day/month/year)* 26/09/1997
Applicant HELISPIN POLARISIERTE GASE GMBH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [ ] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] Transcribed by this Authority

4. With regard to the **title**,
   - [ ] the text is approved as submitted by the applicant
   - [X] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

   Figure No. 1
   - [ ] as suggested by the applicant.
   - [X] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/06056

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G21F5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G21F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 800 158 A (GROSBARD G) 26 March 1974 see claims 1-12; figures 1,9,19 ---	1-9,16, 20-23, 38,45
A	EP 0 540 392 A (THOMSON TUBES ELECTRONIQUES) 5 May 1993 see claims 1-3,5,6; figures 1-3 ---	1-8,18, 20-23, 25-28, 33-38,45
A	US 5 043 529 A (VANESKY FRANK W ET AL) 27 August 1991 see claims 1,5,6,10-14; figures 1-3 -----	1-8,18, 23,39, 40,43,45

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 January 1999	13/01/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Deroubaix, P

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 98/06056

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3800158 A	26-03-1974	NONE	
EP 0540392 A	05-05-1993	FR 2683387 A	07-05-1993
		DE 69202437 D	14-06-1995
		DE 69202437 T	14-09-1995
		JP 6028989 A	04-02-1994
		US 5304792 A	19-04-1994
US 5043529 A	27-08-1991	EP 0467179 A	22-01-1992
		JP 4297227 A	21-10-1992

PATENT COOPERATION TREATY

REC'D 04 JUN 1999
WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
44.43.68617/000		
International application No. PCT/EP98/06056	International filing date (*day/month/year*) 24/09/1998	Priority date (*day/month/year*) 26/09/1997
International Patent Classification (IPC) or national classification and IPC G21F5/00		
Applicant HELISPIN POLARISIERTE GASE GMBH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05/03/1999	01.06.99
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Maugain, C Telephone No. (+49-89) 2399

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/06056

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-24 as originally filed

Claims, No.:

1-47 as originally filed

Drawings, sheets:

1/6-6/6 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-44,47
	No:	Claims	45,46
Inventive step (IS)	Yes:	Claims	1-44,47
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-47
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item I

Basis of the report

4.Additional observation:

It seems that the sole IPC classification G21F5/00 of this application is not sufficient and another classification, for instance, H05K9/00 should be attributed.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1:the article of M EBERT ET AL.: "nuclear magnetic resonance imaging with hyperpolarised helium-3" published in, THE LANCET, 11-05-1996, vol. 347, pages 1297 to 1299.

The document D1 was not cited in the international search report. A copy of this document is appended hereto.

The document D1 is regarded as being the closest prior art to the subject-matter of the independent product claims 1 and 45 and method claim 47, and deals with (cf. p.1297, the right hand column, paragraph **Methods** to p.1298, the left hand column, the two first sentences) , as its title indicates, nuclear magnetic resonance imaging with hyperpolarised helium-3.The polarised and compressed gas ^{3}He is stored in a glass cell....Long relaxation times,up to 100 h in such a cell are achieved by use of specially moulded iron-free Supermax glass, careful cleaning, and eventually an internal coating.The cell is filled...and transported...within a small holding magnetic field for use ....^{3}He samples of 100-300 cm^3 at a presssure of... into the center of the magnet to avoid relaxation by the field gradients in the stray field zone. The measured relative gradient of 4% per cm would cause the polarisation to relax within 50 min.

This document does not disclose a magnetically shielded container as claimed in claim 1 and therefore, the subject matter of claim 1 and of claims 2 to 44, directly or indirectly dependent on claim 1, are new under art.33.2 PCT.

The same conclusion applies to the method claim 47 for the removal of a nuclear spin polarized gas from a gas storage cell in a container as claimed in any one of the

claims 1 to 38; thus, claim 47 is new under art.33.2 PCT.

Document D1 discloses a gas storage cell containing a nuclear spin polarized gas ^3He, as claimed in independent claim 45 and, implicitly, the features of claim 46 dependent on claim 45.Thus, claims 45 and 46 are not new under art.33.2 PCT.

The other available documents and , in particular the documents cited in the search report, are background art documents, which, considered individually or into a combination of their teaching, do not suggest to the skilled person the combination of features of the subject matter of independent claims 1 and 47.

Therefore, the subject matter of claims 1-44 and claim 47 involve an inventive step under art 33.3 PCT.

Re Item VII

Certain defects in the international application

In claims 3-8 ,"...the volume of..." should be deleted;

In claims 6-8, 20-22, 36, 37 "...mL.." or"...kg/L..." should be replaced by "...ml..." or "...kg/l...";

In claim 13 "...in claim 11..." should be replaced by "...in claim 12...";

In claim 37 "...betweem..." should be replaced by "...between..." and "...1 m^3..." by "...1l or1dm^3...";

In the description:

-Page 6, ligne 18 "...between the...and the yoke.";

-from p.8, l.35 to p.9, l.8 the same amendements as for the claims shold be done;

-p.10, l.16 "...by Neil et al..." cf. p.2, l.30;

-p.11, l.20 "...with its axis...";

-p.12, l.13 "...non-limiting examples,...";

-p.13, l. 2 "...made of glass..."; l.19 "...indicated are the...";

-p.14, l.15,16 "...and on the lower disc...and a lower section..."; l.33 "...and the end plate.";

-p.19, l.18 "...with those shown in Figures...";

-p.20, l.18 "Figures...show the..."and

-p.21, l.23 "...T_1^w=70 h.".

D.A
D1

Early reports

Nuclear magnetic resonance imaging with hyperpolarised helium-3

M Ebert, T Grossmann, W Heil, W E Otten, R Surkau, M Leduc, P Bachert, M V Knopp, L R Schad, M Thelen

Summary

Background Magnetic resonance imaging (MRI) relies on magnetisation of hydrogen nuclei (protons) of water molecules in tissue as source of the signal. This technique has been valuable for studying tissues that contain significant amounts of water, but biological settings with low proton content, notably the lungs, are difficult to image. We report use of spin-polarised helium-3 for lung MRI.

Methods A volunteer inhaled hyperpolarised ^{3}He to fill the lungs, which were imaged with a conventional MRI detector assembly. The nuclear spin polarisation of helium, and other noble gases, can be greatly enhanced by laser optical pumping and is about 10^5 times larger than the polarisation of water protons. This enormous gain in polarisation easily overcomes the loss in signal due to the lower density of the gas.

Findings The in-vivo experiment was done in a whole-body MRI scanner. The ^{3}He image showed clear demarcation of the lung against diaphragm, heart, chest wall, and blood vessels (which gave no signal). The signal intensity within the air spaces was greatest in lung regions that are preferentially ventilated in the supine position; less well ventilated areas, such as the apices, showed a weaker signal.

Interpretation MRI with hyperpolarised ^{3}He gas could be an alternative to established nuclear medicine methods. The ability to image air spaces offers the possibility of investigating physiological and pathophysiological processes in pulmonary ventilation and differences in its regional distribution.

Lancet 1996; **347:** 1297–99

Institut für Physik (M Ebert, T Grossmann, W Heil PhD, Prof E W Otten PhD, R Surkau PhD) **und Klinik mit Poliklinik für Radiologie** (Prof M Thelen MD), **Johannes Gutenberg-Universität Mainz, Germany; Ecole Normale Superieure, Paris, France** (M Leduc PhD); **and Forschungsschwerpunkt Radiologische Diagnostik und Therapie, Deutsches Krebsforschungszentrum, Heidelberg, Germany** (P Bachert PhD, M V Knopp MD, L R Schad PhD)

Correspondence to: Dr W Heil, Universität Mainz, Standingerweg 7, Institut für Physik, 55099 Mainz, Germany

Introduction

In 1994 Albert and colleagues[1] demonstrated the possibility of magnetic resonance imaging (MRI) of lung tissue filled with hyperpolarised xenon-129. These investigators then used helium-3 for MRI in a guineapig.[2] The great interest of the medical community in this method arises from the difficulty of imaging porous tissues like the lungs by conventional MRI because of the short T2 and susceptibility differences. Therefore, imaging of lung parenchyma and ventilation has to be done with high-resolution computed tomography enhanced by inhaled xenon as a contrast agent or ventilation scintigraphy with inhalation of radioactive isotopes. Both techniques have the disadvantage of radiation exposure. The noble gases have a great advantage for MRI because they can be hyperpolarised over the ordinary Boltzmann equilibrium of nuclear spin polarisation by means of optical pumping techniques. In a typical magnetic field of 1·5 T, the polarisation is about 5×10^{-6} for protons, but almost 1 in optically pumped noble gases. This enormous gain in polarisation easily overcomes the loss in signal due to the lower density of the gas. We report use of ^{3}He MRI in human beings.

Methods

These results were achieved by use of an advanced technique of polarising large quantities of ^{3}He, which differs from the rubidium spin-exchange technique used by Albert et al.[1,2] Spin-polarised ^{3}He is produced by direct optical pumping from its metastable $^3S_1$ state populated in a low-pressure (0·1 kPa) discharge. The polarisation is transferred with large cross-section through metastability exchange collisions to the nuclei of the ground state atoms; this method therefore has an advantage in terms of production rates.[3] To make full use of this advantage both large laser power and pumping volume are required. The development of arc-lamp-pumped LNA lasers means that about 8 W can be delivered at the desired wavelength of 1·08 μm.[4] We polarise about 6 L of gas within 30 s up to polarisation of about 0·65, corresponding to a production rate of 6×10^{19} polarised spins per second, as required for clinical application of ^{3}He MRI. A convenient pressure of the polarised gas is achieved by a specially developed non-magnetic compression system with moderate polarisation loss.[5,6] The compressed gas is stored in glass cells designed to be detachable and refillable. Long relaxation times (T_1 up to 100 h) in these cells are achieved by use of specially moulded iron-free Supremax glass, careful cleaning, and eventually an internal coating.[7] It takes about 2 h to fill a cell with 100 kPa L; a polarisation of 0·47 of the compressed sample is reached at present. The long relaxation time allows easy storage and handling of the samples. In this experiment the cells were filled in Mainz and transported to the MRI tomograph in Heidelberg within a small holding magnetic field for use of the next day.

All images were acquired in a whole-body NMR scanner (Magnetom 63/84 SP 4000; Siemens, Erlangen, Germany). Since radio-frequency antenna systems for ^{3}He operating at the system's standard field strength of 1·5 T were not available, we used a field strength of 0·79 T and an existing head resonator for 25·8 MHz with two separate loops of diameter 17 cm. ^{3}He samples of 100–300 cm^3 at a pressure of 300 kPa were moved rapidly (about

Figure: **MRI of lungs of volunteer**

Left: proton (^1H) images of tissue water and fatty acid (mainly CH_2) protons recorded at magnetic field 1·5 T (63·6 MHz) with the body-resonator. Right: ^3He images obtained at 0·79 T (25·8 MHz) 28 s after inhalation of hyperpolarized ^3He gas. In-plane spatial resolution was 2·3×2·3 mm² (^1H) and 1·2×1·2 mm² (^3He).

5 s) into the centre of the magnet to avoid relaxation by the field gradients in the stray field zone. The measured relative gradient of 4% per cm would cause the polarisation to relax within 50 min. First tests were done with the ^3He samples themselves serving as phantoms. The signal-to-noise ratio after one excitation with flip angle 1° was about 1000/1; this ratio allowed high-speed MRI with very good quality (fast low angle shot [FLASH]). Because the nuclear polarisation is far above the Boltzmann equilibrium state, every excitation depletes polarisation that cannot be recovered by waiting for a return to equlibrium as usual. Thus, small spin flip angles are mandatory for ^3He pulse sequences; moreover, this approach ensures constant magnetisation during the acquisition of the image.

We undertook an in-vivo ^3He MRI experiment. The thorax of a 27-year-old male volunteer was positioned between the loops of the head resonator and the ^3He sample (300 cm³, pressure 300 kPa) was handed to him. A well-rehearsed ^3He inhalation procedure was initiated; we took into account the effect of oxygen in a normally breathing subject, which would decrease the relaxation time to about 10 s in ordinary air.[9] The volunteer therefore washed out the air from his lungs by taking two breaths of helium-4 gas. Then he took the tip of the ^3He-containing vessel in his mouth, opened the glass valve, and inhaled the polarised sample. Immediately thereafter, multislice two-dimensional FLASH imaging in sagittal orientation was started and repeated three times in rapid succession, while the volunteer held his breath at maximum inspiration (total measurement time 3×28 s). Three sets of seven slices with a field of view of 300×300 mm² were acquired with image matrix 256×256, giving an in-plane spatial resolution of 1·2×1·2 mm²; the resolution in depth is given by the chosen slice thickness of 3 cm. The repetition time of shots was 98 ms with an echo time of 5 ms.

Results

Two corresponding sagittal slices of the lung of the volunteer in the supine position are shown in the figure. The ^3He image (right) shows a sharp demarcation of the lung against diaphragm, heart, chest wall, and blood vessels, which do not give any signal. The signal intensity within the air spaces is proportional to the concentration of ^3He gas. Thus, the regions of the lung that are preferentially ventilated (in the supine position) show maximum signal strength,[12] whereas areas such as the lung apices or the apical parts of the superior segments of the lower lobes show a weaker signal; these findings reflect known physiological regional differences in the ventilation distribution, which can, at least partly, be explained by differences in mechanical stresses.[10,11]

Discussion

Our first ^3He in-vivo experiment on a human being shows that ^3He MRI is a powerful method for imaging air spaces. This technique offers the possibility of investigating physiological and pathophysiological features of pulmonary ventilation and differences in its regional distribution. Mapping of local pulmonary ventilation will become possible. This method will be valuable in the demonstration of regional tissue differences in patients with chronic obstructive pulmonary disease, emphysema, bronchitis, and bronchiolitis.

Mapping of regional ventilation is important in the preoperative assessment of local lung function before thoracic surgery for bronchogenic carcinoma or bulla resection and in diagnostic work-up before volume reduction surgery or single lung transplantation.

After the development of a breathing mask for inhalation and recovery of ^3He, and construction of appropriate radio-frequency antenna systems, this technique will have reached a state ready for clinical research and application.

This experiment was supported by the Human Capital and Mobility Program of the European Union within the network Polarised beams and targets and by the Federal Ministry for Research and Technology in Germany (contract number 03-Ot4MAI). We thank D Hofmann for preparing the transportable ^3He cells; M Bock and H Nilgens for their advice in setting up the ^3He MRI sequences; G van Kaick and W J Lorenz for their support; H Gross and F-P Boroch, Siemens Medical Systems, for technical assistance; and Schott Glaswerke Mainz for producing the special glassware.

References

1 Albert M, Cates GD, Driehuys B, et al. Biological magnetic resonance imaging using laserpolarized ^{129}Xe. *Nature* 1994; 370: 199–201.

2 Middleton H, Black RD, Saam B, et al. MR ima[illegible] with hyperpolarized ^{3}He gas. *Magnetic Resonance Med* 1995; 33: 271–75.
3 Eckert G, Heil W, Meyerhoff M, et al. A dense polarized ^{3}He target based on compression of optically pumped gas. *Nucl Instr Meth A* 1992; 320: 53–65.
4 Aminoff CG, Larat C, Leduc M, Laloë F. Optical pumping of helium with arc lamp excited LNA lasers. *Rev Phys Appl* 1989; 24: 827–31.
5 Becker J, Heil W, Krug B, et al. Study of mechanical compression of spin-polarized ^{3}He gas. *Nucl Instr Meth A* 1994; 346: 45–51.
6 Heil W, Surkau R. Development of a dense polarized ^{3}He spin filter based on compression of optically pumped gas. *J Neutron Res* (in press).
7 Heil W, Humblot H, Otten EW, Schäfer M, Surkau R, Leduc M. Very long nuclear relaxation time[illegible]n polarized helium 3 in metal coated cells. *Phys Lett A* 1995; 201: 337–43.
8 Haase A, Frahm JA, Matthaei D, Merbolt K-D. FLASH imaging. Rapid NMR imaging using low flip-angle pulses. *J Magn Reson* 1986; 67: 258–66.
9 Saam B, Happer W, Middleton H. Nuclear relaxation of ^{3}He in the presence of O_2. *Phys Rev A* 1995; 52: 862–65.
10 West JB. Distribution of mechanical stress in the lung: a possible factor in localisation of pulmonary disease. *Lancet* 1971; i: 839–44.
11 West JB, Matthews FL. Stresses, strains and surface pressures in the lung caused by its weight. *J Appl Physiol* 1972; 32: 332–40.

Congenital enterocyte heparan sulphate deficiency with massive albumin loss, secretory diarrhoea, and malnutrition

Simon H Murch, Paul J D Winyard, Sibylle Koletzko, Birgit Wehner, Huma A Cheema, R Anthony Risdon, Alan D Phillips, Nigel Meadows, Nigel J Klein, John A Walker-Smith

Summary

Background The molecular basis of protein-losing enteropathy is unknown. However it has been shown that sulphated glycosaminoglycans may be important in regulating vascular and renal albumin loss.

Methods We describe three baby boys who presented within the first weeks of life with massive enteric protein loss, secretory diarrhoea, and intolerance of enteral feeds. All required total parenteral nutrition and repeated albumin infusions. No cause could be found in any case despite extensive investigations, including small intestinal biopsy sampling, which were repeatedly normal.

Findings By specific histochemistry, we detected gross abnormality in the distribution of small intestinal glycosaminoglycans in all three infants, with complete absence of enterocyte heparan sulphate. The distribution of vascular and lamina propria glycosaminoglycans was, however, normal.

Interpretation The presentation of these infants suggests that enterocyte heparan sulphate is important in normal small intestinal function.

Lancet 1996; **347:** 1299–301

University Department of Paediatric Gastroenterology, Royal Free Hospital, London NW3 2QG, UK (S H Murch PhD, D Phillips PhD, Prof J A Walker-Smith FRCP); **Queen Elizabeth Hospital for Children, London** (P J D Winyard MRCP, N Meadows FRCP); **Kinderpoliklinik, University of Munich, Germany** (S Koletzko MD, B Wehner MD); **Department of Pediatrics, King Saud University Hospital, Abha, Saudi Arabia** (H A Cheema MRCP); **Department of Histopathology, Hospital for Sick Children, London** (Prof R A Risdon FRCPath); **and Molecular Immunology Unit, Institute of Child Health, London** (N J Klein MRCP)

Correspondence to: Dr Simon H Murch

Introduction

Retention of proteins within the vasculature or tissue compartments is dependent upon both their molecular radius and electrostatic charge.[1] Thus reduction of endothelial anions, particularly sulphated glycosaminoglycans (GAGs) by cations or enzymatic degradation, greatly increases albumin and water leakage.[2] Similar mechanisms may induce urinary albumin loss in congenital and minimal lesion nephrotic syndromes.[3] However, very little is known about the physiological role of GAGs at other epithelial surfaces.

Degradation of sulphated GAGs might occur as a specific consequence of inflammation, potentially contributing to vascular leak.[4] We have shown loss of sulphated GAGs from the epithelium and basement membrane in inflamed intestine, and have suggested that this may be the mechanism of intestinal protein loss in inflammatory enteropathy.[5,6] We now report three infants with congenital absence of enterocyte heparan sulphate who had profound enteric protein loss with secretory diarrhoea and absorption failure, despite having uninflamed, histologically normal intestines.

Patients and methods

Clinical details of the three affected infants, all of whom were first-born boys from non-consanguineous families, are given in the table. Cases 1 and 2 presented with severe symptoms within the first days of life and died in infancy. Case 3 was less severely affected, and remains alive at 2 years.

Case 1

This British baby developed diarrhoea with rectal bleeding at 10 days and was found to have serum albumin less than 6 g/L with no proteinuria. Reintroduction of feeds led to worsening diarrhoea and peripheral oedema. Enteric albumin loss was found (table), and labelled albumin scan showed diffuse accumulation within the small intestine. All other investigations were normal. By 6 weeks, he was 700 g below birthweight, with persistent diarrhoea and requirement for albumin and electrolyte infusion. Small-bowel biopsy samples were histologically normal on three occasions. Electron microscopy excluded microvillous atrophy and demonstrated minor thickening of the subepithelial basement membrane.

Despite total parenteral nutrition (TPN), his symptoms persisted, and worsened on any oral intake. Faecal α-1-

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/06056

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G21F5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G21F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 800 158 A (GROSBARD G) 26 March 1974 see claims 1-12; figures 1,9,19 ---	1-9,16, 20-23, 38,45
A	EP 0 540 392 A (THOMSON TUBES ELECTRONIQUES) 5 May 1993 see claims 1-3,5,6; figures 1-3 ---	1-8,18, 20-23, 25-28, 33-38,45
A	US 5 043 529 A (VANESKY FRANK W ET AL) 27 August 1991 see claims 1,5,6,10-14; figures 1-3 -----	1-8,18, 23,39, 40,43,45

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 January 1999	13/01/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Deroubaix, P

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 98/06056

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
US 3800158	A	26-03-1974	NONE			
EP 0540392	A	05-05-1993	FR	2683387	A	07-05-1993
			DE	69202437	D	14-06-1995
			DE	69202437	T	14-09-1995
			JP	6028989	A	04-02-1994
			US	5304792	A	19-04-1994
US 5043529	A	27-08-1991	EP	0467179	A	22-01-1992
			JP	4297227	A	21-10-1992

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 44.68617/000	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 98/06056	International filing date *(day/month/year)* 24/09/1998	(Earliest) Priority Date *(day/month/year)* 26/09/1997
Applicant HELISPIN POLARISIERTE GASE GMBH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [ ] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] Transcribed by this Authority

4. With regard to the **title**,
   - [ ] the text is approved as submitted by the applicant
   - [X] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

   Figure No. 1
   - [ ] as suggested by the applicant.
   - [X] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/06056

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G21F5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G21F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 800 158 A (GROSBARD G) 26 March 1974 see claims 1-12; figures 1,9,19 ---	1-9,16, 20-23, 38,45
A	EP 0 540 392 A (THOMSON TUBES ELECTRONIQUES) 5 May 1993 see claims 1-3,5,6; figures 1-3 ---	1-8,18, 20-23, 25-28, 33-38,45
A	US 5 043 529 A (VANESKY FRANK W ET AL) 27 August 1991 see claims 1,5,6,10-14; figures 1-3 -----	1-8,18, 23,39, 40,43,45

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 January 1999	13/01/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Deroubaix, P

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 98/06056

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
US 3800158	A	26-03-1974	NONE			
EP 0540392	A	05-05-1993	FR	2683387	A	07-05-1993
			DE	69202437	D	14-06-1995
			DE	69202437	T	14-09-1995
			JP	6028989	A	04-02-1994
			US	5304792	A	19-04-1994
US 5043529	A	27-08-1991	EP	0467179	A	22-01-1992
			JP	4297227	A	21-10-1992

MAGNETICALLY SHIELDED CONTAINER

The invention relates to a magnetically shielded container, e.g. usable as a transport device for spin polarized gases, and to a storage cell useful therein.

Nuclear spin polarized gases, in particular noble gases such as the helium isotope with the mass number 3 (^3He) or the xenon isotope with the mass number 129 (^{129}Xe) and gases containing the fluorine, carbon or phosphorus isotopes ^{19}F, ^{13}C or ^{31}P are required for a great number of experiments in fundamental physics research. In the field of medicine, such isotopes are, in particular, considered for use in nuclear magnetic resonance imaging, of the lungs for example. (See for example WO 97/37239, WO 95/27438, Bachert et al., Mag Res Med <u>36</u>: 192-196 (1996) and Ebert et al., The Lancet <u>347</u>: 1297-1299 (1996)). A prerequisite for the use of such spin polarized gases in nuclear magnetic resonance imaging is that the degree of polarization P of the spin I of the nuclei, or the associated magnetic dipole moment μ_I, is greater by an order of 4-5 than is normally achieved in thermal equilibrium in the magnetic field B_T of the magnetic resonance imaging apparatus. This normal degree of polarization, $P_{Boltzmann}$, is dependent on the magnetic dipole energy $-\mu_I B_T$ and average thermal energy kT:

$$P_{Boltzmann} = \tanh\ (\mu_I B_T/kT) \qquad (1)$$

(where k = Boltzmann's constant, and T = absolute temperature).
Where $P_{Boltzmann} << 1$, then it approximates to $\mu_I B_T/kT$.

Whereas the hydrogen isotope ^1H used in magnetic resonance imaging of tissues only reaches a $P_{Boltzmann}$ of 5

x 10^{-6} at B_T = 1.5 T and T = 300 K, a P≥ $1x10^{-2}$, i.e. 1%, is required in gas magnetic resonance imaging. The requirement for such an extremely increased P primarily results from the low concentration of the gas atoms in comparison with that of the hydrogen in the tissue. Gases with such degrees of polarization (normally referred to as hyperpolarized gases) can be produced by means of various known methods, preferably optical pumping.

In addition, for gas magnetic resonance imaging relatively large quantities of gas, of the volume of a breath for example (0.5 to 1 litre), are needed.

Particularly high degrees of polarization, for example >30%, combined with high rates of production, e.g. 0.5 litres/h, may be achieved through compression of an optically-pumped gas. This process is described in the following publications, the content of which is incorporated herein by reference:

- Eckert et al., Nuclear Instruments and Methods in Physics Research A 320: 53-65 (1992);
- Becker et al., J. Neutron Research 5; 1-10 (1996);
- Surkau et al., Nuclear Instruments and Methods in Physics Research A 384: 444-450 (1997);
- Neil et al., Physics Letters A 201: 337-343 (1995).

However production and use of hyperpolarized gases do not necessarily occur at the same site and the problem thus arises of transporting the polarized gases, produced for example using the method described above, to the consumer, for example for use in a nuclear magnetic resonance imaging apparatus for the lungs.

Previously, transportable magnetic devices which provide a sufficiently homogeneous magnetic holding field for a large storage volume of such a spin polarized gas were not available. Furthermore, the nuclear spins very rapidly depolarized on the cell walls, so that polarized gases could only be stored for a short time while retaining the necessary degree of polarization.

One problem addressed by the invention is to provide a magnetic device capable of providing a transportable, homogeneous magnetic holding field for a sufficiently large storage volume of hyperpolarized gas.

Viewed from one aspect the invention thus provides a magnetically shielded container having disposed in parallel opposed position on an axis thereof magnetic field homogenizing pole shoes, having disposed about said pole shoes a magnetically shielding yoke, said pole shoes and yoke enclosing a magnetic chamber, said container further comprising magnetic field sources disposed about and radially distanced from said axis whereby there exists within said chamber a substantially homogeneous magnetic field B_o oriented in the direction of said axis and whereby there is a usable volume within said chamber where the ratio of the magnetic field gradient in the direction transverse to said axis to said magnetic field B_o has a value of no more than 1.5×10^{-3}/cm.

Such a container may be constructed in a form which is low in weight, simple in structure, and inexpensive to manufacture and economical in use. Furthermore, using the container, nuclei which are transported can, as far as possible, retain their orientation, even in external stray fields, i.e. the depolarization relaxation times may be as long as possible in order to prevent a disorientation of the nuclear spin of.the gas.

The container of the invention, which is suitable for containing and transporting spin polarized atoms, especially polarized ^3He and ^{129}Xe, is preferably provided with magnetic field homogenising, highly-permeable and magnetically soft plates, e.g. of μ-metal or soft iron, as pole shoes, and is so structured that a very large ratio can be achieved between the usable volume, within which a sufficiently homogeneous magnetic field is present, and the total volume, e.g. a ratio of at least 1:30. However, this ratio is preferably at least 1:5, more preferably 1:3 and, particularly advantageously 1:2. A ratio of 1:1.5 can be achieved. A value of

$$G_r = ((\delta B_r/\delta r)/B_o) \leq 1.5 \times 10^{-3}/cm \quad (2)$$

is hereby applied as a homogeneity condition within the usable volume for the relative transverse gradient G_r of the magnetic field B_o. This requirement results from the gradient-dependent relaxation time T_{1G}, which (at high pressures, such as those the present invention is concerned with) is related as follows to G_r and the gas pressure p:

$$T_{1G} = p/G_r^2 \times (1.75 \times 10^4 \ cm^2bar/h)^{-1} \quad (3)$$

(see Scherer et al., Phys Rev <u>139</u>: 1398 (1965)).

According to equation (3), with $G_r < 1.3 \times 10^{-3}/cm$ and p = 3 bars, a gradient-dependent relaxation time $T_{1G} > 76$ h is achieved.

At lower pressures, $T_{1G} = p/G_r^2 \times (1.8 \times 10^3 \ cm^2bar/h)^{-1}$ (see Barbe, Journal de Physique <u>35</u>: 699 and 937 (1974)).

During the movement of a polarized gas storage cell into the container of the invention, G_r will generally be less than $0.02 \times 10^{-3}/cm$. In this way ^3He at 3 bar loses only

2% polarization per 30 seconds.

Within the container according to the invention, G_r is preferably no more than 1.3×10^{-3}/cm, more preferably no more than 7×10^{-4}/cm. With a gas storage cell radius of 8 cm, G_r of $\leq 1.3 \times 10^{-3}$/cm corresponds to T_{1G} of ≥ 127 hours, while with a gas storage cell radius of 2 cm, G_r of $\leq 7 \times 10^{-4}$/cm corresponds to T_{1G} of ≥ 350 hours.

In order to compensate field distortions in the marginal areas of the interior space of the container and thus improve the homogeneity of the magnetic field B_o, the container features magnetic field sources which are arranged in such a way that the field distortions in the marginal areas of the interior space of the container are minimal and the field in the interior of the container is largely homogeneous.

In order to maintain the polarization of the nuclear spin once it has been achieved, only a relatively weak homogeneous magnetic field is required which preferably displays a magnetic field strength of less than 5 mT, more preferably less than 1 mT, more especially in the range 0.2 to 0.9 mT. In such a weak magnetic field, continuous quality control of the degree of polarization can be achieved with the aid of measuring instruments, ensuring particular reliability. Thus in one preferred embodiment, a magnetic field sensor (e.g. one based on the Förster principle) is disposed in the container of the invention so as to allow determination of the magnetic field B_d generated by the hyperpolarized gas.

Whereas the generation of strictly homogeneous magnetic fields with the aid of ferromagnetic materials previously concentrated on high field strengths within the tesla range, the concept behind the container of the invention is deliberately focused on the most efficient

and practical realisation of a weak, widely homogeneous magnetic field, e.g. using ferromagnetic materials.

A high degree of homogeneity can be achieved within the weak field range if, for example, as homogenising ferromagnetic elements, two thin soft iron, or more preferably μ-metal, plates are used as pole shoes. Such pole shoes, thanks to their extremely high permeability and low remanence, create a very homogeneous field within the intervening space, the magnetic chamber.

In a particularly preferred embodiment, the homogenising effect of these pole shoes can be increased by introducing magnetic resistances between the pole shoes and the yoke. A preferred material for a magnetic resistance of this sort, is a rigid non-magnetic layer, for instance in the form of a plate, for example of plastic, fitted between the pole shoe and yoke. If such a plate or, in order to save weight, preferably a porous, e.g. honeycomb structure, is also bonded to the pole shoe, this guarantees its flatness which allows the pole shoes to be parallel and the field B_o to be homogeneous.

In order to fulfil the aforementioned homogeneity conditions in the simplest possible manner, and at the same time to provide a large storage volume, it has proved especially preferable to design the container of the invention in the form of a pot magnet. A magnetic device of this sort consists essentially of a closed pot which, in an exemplary construction form, can have a diameter of 30-60 cm with an overall height of 10-30 cm. The particular advantage of designing the container in the form of a pot magnet lies in the high degree of symmetry of this cylindrical construction. Two possibilities can be considered as particularly preferred arrangements of the field sources in a pot

magnet of this sort:

- positioning the field sources, for example in the form of commercially-available permanent magnetic plates, in a gap in the median or reflection plane of the pot; and

- positioning the field sources on the outer surface of the end plates of the pot.

By appropriately dividing the field sources between these two arrangements, on the one hand positioning the field sources in the median plane, on the other hand positioning the field sources on the outer surface of the end plates of the pot, it is possible to correct the boundary errors of the magnetic field inside the pot magnet and thus fulfil the homogeneity conditions over a wide range in a radial direction. A preferred division is such that the increase in the boundary field which occurs when the field sources are arranged in the reflective or median plane of the pot magnet is just compensated by the fall-off in the boundary field which occurs where the field sources are positioned on the end plate of the pot.

If desired, magnetic field sources may be placed elsewhere in the container of the invention so as to achieve an improvement in the homogenization of the applied field B_o. Thus for example such sources may be placed in further planes perpendicular to B_o besides the planes of, adjacent to and mid-way between the pole shoes.

A particularly homogeneous boundary field is also achieved if a magnetic screen, e.g. a soft iron or μ-metal ring, is fitted between the pot and the rim of the pole shoe, so that an external stray field is partially

short-circuited and, where the field sources are arranged on the median plane of the pot magnet, the value of the boundary field is reduced to the value of the central field in the centre of the pot magnet through appropriate dimensioning of the magnetic screen.

Advantageously, especially in the case of non-circular cylindrical (e.g hexagonal-cylindrical) containers according to the invention, shims (e.g. corner shims-positioned onto the pole shoes) may be used to improve field homogeneity within the magnetic chamber. Advantageously also the chamber has a high degree of azimuthal symmetry.

Two preferred construction forms can be used as magnetic field sources. In a first construction form, permanent magnets can be used, preferably commercially-available tablets, for example with a height of 5 mm and a diameter of 20 mm. In another construction form, these permanent magnets are replaced with appropriately-dimensioned magnetic field coils. Such magnetic field coils have the advantage that the desired magnetic fields can be adjusted by means of an appropriately-selected current flow. However, a disadvantage of the second construction form is that an additional current source must be carried with the container where it is used as a transport device rather than simply as a storage device.

The container is advantageously constructed using a yoke of a material which is not magnetically saturated at fields below 1 Tesla, more preferably 2 Tesla, e.g. a soft iron. The container dimensions are preferably such that the usable volume (within which the gas storage cell may be disposed) is at least 50 mL, more preferably 100 mL, especially preferably 200 mL to greater than 1 m^3, e.g. up to 20L, more particularly 200-2000 mL. The

materials used can allow a total container weight to magnetic chamber volume of no more than 1 kg/L, more preferably 0.2 kg/L, especially preferably 1/30 kg/L. The gas storage cell which can be disposed in the container, e.g. for storage or transport, preferably has an internal volume of at least 50 mL, e.g. 100 mL to 1 m^3, particularly 100 mL to 20L, more particularly 200 mL to 2L. This cell may be provided with a valve for allowing gas introduction and removal; alternatively it may be a single-use cell, e.g. provided with a sealable portion and a breakable portion (which may be the sealable portion after sealing).

In one embodiment, the container of the invention may take the form of a magnetic device with an internal space which provides a high-volume, largely homogeneous, shielded magnetic field within its interior, whereby the magnetic device features homogenising μ-metal plates as pole shoes, the magnetic device is characterised in that a ratio of 1:1.5 can be achieved between the useable volume of the magnetic device within which a homogeneous magnetic field is present and the overall volume of the magnetic device and the homogeneity condition

$$G_r \leq 1.5 \times 10^{-3}/\text{cm}$$

is fulfilled within the useable volume, where G_r is the relative transverse magnetic field gradient.

Viewed from a further aspect, the invention also provides a gas storage cell containing a nuclear spin polarized gas in a gas storage space surrounded by a cell wall, the wall being of an uncoated material which on the surface contacting said gas storage space is substantially free of paramagnetic substances. The gas may for example be ^3He or ^{129}Xe, especially ^3He. Using an essentially paramagnetic substance free cell wall makes

it possible for polarized ^3He to display a wall-related depolarization relaxation time T_1^w of at least 20 hours. It is particularly preferable that the wall-related depolarization relaxation time be more than 50 hours. Such high depolarization relaxation times can be achieved if a material is used as cell wall material which contains a low proportion of paramagnetic atoms or molecules, whereby in a particularly preferred construction form glasses with very low iron concentrations, preferably less than 20 ppm, are used, which can also be composed in such a way that, at the same time, they represent an efficient diffusion barrier against helium, for example Supremex glass (manufactured by Schott, Mainz, DE) of the type of the alumina silicate glasses. In comparison with the previously-known storage cells described by Heil et al. in Physics Letters A 201: 337-343 (1995), long wall-related depolarization relaxation times can be achieved using the storage cells in accordance with the invention, without complex metal coating of the walls being necessary.

As mentioned above, the container of the invention may take the form of a transport device for spin polarized gases, especially ^3He and ^{129}Xe or gases containing ^{19}F, ^{13}C or ^{31}P, e.g. gases which have been spin polarized by polarization transfer. Within the area in the interior space of the container in which the storage cell is positioned, the magnetic field of the magnetic device can be so homogeneous that the depolarization relaxation time T_1^g caused by a transverse magnetic field gradient in accordance with equation (3) is greater than 125 hours, especially greater than 200 hours, more particularly greater than 300 hours, preferably greater than 500 hours, particularly preferably greater than 750 hours, and the wall-related depolarization relaxation time T_1^w, due to impacts of the nuclear-polarized gas on

the wall of the storage cell, is greater than 5 hours, preferably greater than 20 hours.

More preferably, T_1^w normalized by the interior surface to volume ratio of the storage cell is preferably at least 10 h/cm.

However, depolarization losses occur not only during the transport of the gas, due to the influence of external stray magnetic fields and the resulting inhomogeneity of the magnetic field, or due to collisions between the atoms and the wall, but, in particular, also when the gas is removed from the transport container.

Viewed from a still further aspect, the invention therefore provides a method for the removal of a nuclear spin polarized gas from a gas storage cell in a container comprising:

(i) positioning said container with said axis parallel to the field direction of an external substantially homogeneous magnetic field;

(ii) opening said container by removing a portion comprising one of said pole shoes; and

(iii) removing said cell in the direction of said axis.

Such depolarization losses can be minimised if the removal of the polarized gas takes place according to this method.

In this method, the container, e.g. in the form of a pot magnet, is set up with its axis and the alignment of the internal, homogeneous magnetic field parallel to an external, adequately homogeneous magnetic field, which can, for example, be achieved with the aid of a Helmholz

coil or the stray field of a nuclear magnetic resonance imaging apparatus. The half of the pot magnet facing the homogeneous magnetic field in an axial direction is then lifted off. The remaining half then guarantees a sufficient field homogeneity in the area of the gas cell through the magnetic equipotential surface of its pole shoe, which is made, for instance, of μ-metal. The removal of the storage cell filled with polarized gas from the magnet can take place in an axial direction within a few seconds.

Embodiments of the invention are described by way of non-limiting Examples, with reference to the accompanying drawings, in which:

Fig. 1: shows an external perspective view of the container of the invention;

Fig. 2: shows a cross section through a container in accordance with the invention, which is in pot magnet form and contains a storage cell for spin polarized gases positioned within its interior;

Figs. 3a-d: show various arrangements for boundary field compensation;

Fig. 4: shows a further variant of the container in accordance with the invention;

Fig. 5a: shows the curve of the value of the relative, radial gradient G_r in the radial direction R of a pot magnet for different arrangements of the field sources;

Fig. 5b: shows the curve of Figure 5a with the scale modified for emphasis;

Fig. 6: shows the relaxation of ^3He polarization in a storage cell made of of glass with a low iron content, whereby the volume of the cell is, for example, 350 cm^3 and the gas pressure 2.5 bars;

Figs. 7a-b: demonstrate the removal of a storage cell from a container according to the invention placed within an external field; and

Fig. 8: shows a further variant of a container according to the invention which has non-circular cylindrical symmetry.

Referring to Figure 1, there is shown an external perspective view of a container 1 in accordance with the invention, which in this instance is designed as a two-part cylindrical pot magnet with an upper section 1.1 and a lower section 1.2. Also indicated is the rotationally symmetrical axis S of the pot magnet and the magnetic field line of external magnetic fields, for example the earth's magnetic field. Especially clearly shown is the path of an external magnetic field or stray field $B_s^{\perp}$ which does not penetrate into the interior of the pot magnet but, due to the slight magnetic resistance of the yoke 2, which is preferably made of soft iron material, is conducted around the interior space. The stray field B_s^{II} is perpendicular to the end-plates of the yoke and is homogenised by the μ-soft iron pole shoes positioned inside the yoke 2.

Figure 2 shows an axial cross section through a container for spin polarized gases, especially ^3He, ^{129}Xe, as shown in Figure 1, comprising the container in accordance with the invention and a storage cell for spin polarized gas positioned inside it, which is characterised by extremely long wall depolarization

relaxation times.

The pot magnet 1 comprises a cylindrically-formed yoke 2, preferably made of soft iron for returning the magnetic flux and for shielding off external fields. In turn, the cylindrically-formed yoke 2 features two yoke end plates forming a central section 2.1. In the construction form shown, the yoke end plates 2.1 take the form of two circular discs 2.1.1 and 2.1.2. Closed surrounding sheets 2.2 and 2.3 are arranged around the rim of the yoke end plates to form a yoke jacket. These differ in the two construction forms shown in the left and right halves of Fig. 2. The surrounding sheets 2.2 and 2.3 are arranged both on the upper disc 2.1.1 and also on the lower disc 2.1.2, resulting in an upper section and lower section of the pot magnet, which, in the first construction form shown on the left, meet at the projecting angled peripheral flanges 2.2.1 in the median plane of the magnetic device. In the second construction form shown on the right, the peripheral flanges 2.3.1 are spaced in such a way that an opening for holding field sources, for example permanent magnets, is formed in the median plane 4 of the pot magnet 1. The field line produced due to the positioning of the field sources, for example the permanent magnets, in the centre between the upper and lower peripheral flanges of the pot magnet is identified with 6. In the first construction form shown on the left, the height of the two halves of the yoke jacket 2.2 exceeds the distance between the yoke end plates 2.1.1, 2.1.2. It is possible to position field sources on the outer surface 2.5 in the gap between the jacket and end plate. The field line in the boundary region which results with such an arrangement is identified with the number 8.

The two opposing pole shoes 10.1 and 10.2 are

responsible for the homogeneous field within the interior of the pot magnet. In this example, the pole shoes are essentially designed as homogenising μ-metal plates. μ-metal is a material with a very high homogenising force in relation to an external, stray magnetic field B_x^{II} and is distinguished by very low remanences.

In this example, μ-metal A manufactured by Vacuumschmelze, P.O. Box 2253,63412 Hanau with the following magnetic characteristics is used:

Stat. coercivity:	H_c	$\leq$ 30 mA/cm
Permeability:	$\mu_{(4)}$	$\geq$ 30,000
Maximum permeability:	$\mu_{(max)}$	$\geq$ 70,000
Saturation inductance:	B_2	$\geq$ 0.65 T

(This should not be interpreted as meaning that only this material can be used for the invention). Over the entire pole shoes, the distance between the shoes, and the parallel orientation of the pole shoes may be ensured by the provision of spacer elements or spacer rings, e.g. a total of three (or more) spacers 12, of which only one is shown in Figure 2.

The resulting homogeneous magnetic field between the pole shoes 10.1 and 10.2, made of μ-metal, is identified with the reference number 14 in this representation. As can be seen from the representation in Figure 1, a particularly homogeneous magnetic field, independent of external fields, is achieved inside the pot magnet due to the homogenising force of the μ-metal, whereas, in the marginal areas, depending on the arrangement of the field sources, a different field pattern 6 or 8 occurs. If the field sources are arranged solely in the median plane 4, as shown for the right-hand marginal area of the pot magnet 1, then a considerable part of the

magnetic flux escapes from the jacket due to the low magnetic resistance and, acting from the edge, interferes with field between the pole shoes, with an amplifying effect. The field therefore increases significantly in intensity towards the edge, as a result of which the desired homogeneity is impaired even where the two pole shoes are a relative short distance apart. Where the permanent magnets are positioned on the outer surface on the end plates of the pot, as shown in Figure 2 for the left-hand half of the magnet, a significant marginal fall-off of the field is observed between the pole shoes 10.1,10.2, as shown by the field line 8, because the jacket, which reaches right up to the pole shoes, attracts and weakens the boundary field.

The very homogeneous field 14 produced in the intervening space due to the extremely high permeability of the μ-metal plates used as pole shoes 10.1,10.2 can be increased even further through the introduction of a magnetic resistance 16 between the pole shoes 10.1, 10.2 and the yoke 2.1.1 and 2.1.2. A rigid, non-magnetic plate, for example a plastic plate 16 or, in order to save weight, preferably a honeycomb structure, is preferably used for this purpose. The plate 16 can be bonded to the pole shoes 10.1,10.2, thus guaranteeing the flatness of the pole shoes 10.1,10.2.

The storage cell 20 for holding the polarized gas is located in the central mid-section of the pot magnet 1 between the two pole shoes 10.1,10.2. The container 20 is preferably manufactured of iron-free glass and has an iron concentration of less than 20 ppm, for example, and can also be designed in such a way that it also forms an efficient diffusion barrier against helium. This measure allows wall-related relaxation times of more than 70 hours to be achieved. The storage cells 20 can be pumped out prior to use and, for example, as is usual

in high-vacuum technology, heated through until their residual water layers are lost. This measure is advantageous in the invention, but by no means necessary. The storage cells are, for example, sealed with a glass stopcock 22 and are connected to the filling unit for the polarized gas via a glass flange 24.

In addition, in order to determine the degree of polarization, a high-frequency coil 30 (which can be used to subject the storage cell 20 to a time-variant magnetic field) and a detection device (e.g. a magnetic field sensor) 32 can be fitted as may means for moving sensor and storage cell relative to each other. However, these additional fixtures are optional and are by no means essential for a transport device in accordance with the invention.

Furthermore, the container may if desired be fitted with cooling means to cool the contents of the gas storage cell.

The decisive feature of the invention is that a magnetic field is created within the container which is homogeneous over a very large volume, so that a high usable volume is achieved in relation to the total volume of the magnetic device, whereby the homogeneous field within the interior of the magnetic device is essentially not to be interfered with by external magnetic fields. On the one hand, the low magnetic field strength of $B_0 < 1$ mT which may be used allows a very lightweight construction of the yoke and pole shoes using thin soft iron sheeting. On the other hand, it is desirable that the pole shoes display particularly low remanence, so that these are therefore preferably made of μ-metal in order to fulfil the homogeneity requirement (2).

In terms of being able to determine the degree of polarization, it is advantageous if the homogeneous holding field in the interior of the magnet is a weak magnetic field with a field strength of less than 1.0 mT, since the magnetic fields caused by the spin polarization of the gas, which lie within the nano to micro Tesla range, can then still be measured with sufficient accuracy with the aid of the simple detection device 32 and the degree of polarization determined on this basis. This is advantageous if, for example, the quality of the delivered gas has to be tested prior to a medical application.

Figure 3 shows the field distribution within the marginal area achieved by means of different arrangements of field sources, either alone or in combination with a magnetic screen, which guarantees a sufficiently homogeneous field distribution within the marginal area.

Figure 3a shows an arrangement in which the permanent magnets are placed inside the gap 2.4 and inside the gap 2.5 on the end plates of the pot 2.1.1, 2.1.2. By dividing the arrangement of the permanent magnets 2.4. appropriately between arrangement in the centre 4 and arrangement on the end plates of the pot 2.1.1, 2.1.2, the increase in the intensity of the boundary field 6, which is caused by the positioning of the permanent magnets in the centre between the end plates of the pot, as shown, is just compensated by the fall-off in the intensity of the boundary field 8 of the permanent magnets arranged on the end plates of the pot. If the individual permanent magnets are of equal magnetic field strength, an optimal distribution of the permanent magnets is achieved, for the height-to-width ratio of the pot shown in the drawing, if the magnets are distributed in a numerical ratio of 6:8, whereby the

first figure represents the number of magnets which are arranged in the median plane 4, and the second figure represents the number of magnets which are arranged on the end plates of the pot.

Figure 3b shows a possible homogenisation of a boundary field using permanent magnets arranged in the median plane 4 with the aid of a magnetic screen 40. A magnetic screen of this sort is, for example, formed by a soft iron ring which is introduced between the pot and the rim of the pole shoe and which, like the sheets 2.2,2.3, runs around it. Such a soft iron ring partially short-circuits the stray external field and, if appropriately dimensioned, reduces the boundary field to the value of the central field.

Figures 3c and 3d show means of compensation which are comparable with Figures 3a and 3b where, in this example, magnetic coils 50,52 arranged centrally in the area of the median plane 4 of the pot or in the vicinity of the end plates of the pot are used as field sources instead of permanent magnets.

Figure 3c shows the compensation achieved through a suitable ratio of field sources arranged in the median plane to field sources arranged in the vicinity of the end plates of the pot, and Figure 3d shows the compensation with the aid of a magnetic screen 40.

A further construction form of the invention is shown in Figure 4. In order to reduce weight, the yoke jacket is constructed of very thin surrounding sheets 200.1,200.2 and 202.1 and 202.2, in a double-walled construction. The surrounding sheets 200.1, 200.2 and 202.1 and 202.2 are arranged at a fixed distance from one another using spacing rings 207, so that a double shielding of the interior of the pot magnet 1 is achieved. These can be

considerably thinner than in a single-walled construction form as shown in Figure 1, while displaying the same capacity to conduct magnetic fluxes away via the shielding rings. The surrounding sheets are connected with the upper or lower μ-metal plate of the pot magnet via a screwed connection 204 or 206. The pole shoes 10.1 and 10.2 are spaced apart by means of spacing elements or a spacing ring 205 which may be circular or polygonal, e.g. hexagonal, in cross-section. The homogeneous magnetic field is essentially formed in the interior 208 between the pole shoes. As in Figure 3a, the permanent magnets 210 fitted in the gap 2.4 between the upper and lower section of the pot magnet and between the jacket and end plate serve as sources for a field which is also homogeneous in the marginal area.

Figures 5a and 5b shows the curve of the amount of the relative, radial gradient $G_r = ((\delta B_r/\delta_r)/B_o)$ measured 1.5 cm above the reflective plane 4 of the pot magnet in a radial direction r for different arrangements of the permanent magnets in or on the pot magnet in accordance with the invention. The curve marked "a" shows the curve produced when permanent magnets are only arranged in the gap in the median plane 4, as shown in the right half of Fig. 2, and the curve marked "b" shows the curve produced where the permanent magnets are positioned on the outer surface on the end plates of the pot as shown on the left-hand side of Fig. 2. The curve identified with "c" shows the curve of the radial gradient which is produced if the permanent magnets are divided between being positioned on the outer surface and being positioned in the gap in the median plane in accordance with Fig. 3a. The numerical ratio between the magnets is 6:8 in the curve shown in curve 3c, i.e. 6 magnets were arranged in the centre and 8 on the end plates. In this case, with a gap between the pole shoes of 18 cm

and a pole shoe diameter of 40 cm, the homogeneity limit which is represented by the dotted band 400 achieves a value of $G_r = 1.5 \times 10^{-3}$ with r approximately 13 cm, more preferably 12 cm. This limit 400 is displayed over the entire height of the pot magnet, so that a usable transport volume of more than 6 litres, e.g. more than 8 litres is provided within the pot magnet, in which the homogeneity condition $G_r \leq 1.5 \times 10^{-3}$/cm is fulfilled.

Figure 6 shows a measurement record of the relaxation of the ^3He polarization in a storage cell of glass with a low iron content. The volume of the storage cell is 350 cm^3, the gas pressure 2.5 bars. As can be seen from this figure, a relaxation time of more than 70 hours is measured through the use of such glasses, whereby the gradient-dependent relaxation time could be ignored under the conditions for this measurement. If one introduces such a receptacle consisting of glass with a low iron content into the pot magnet in the region of the homogenised field, a resulting total relaxation time $T_{res} = (1/T_1^g + 1/T_1^w)^{-1}$ of 64 hours is achieved, based on a gradient-dependent relaxation time of T_1^g = 750 h and a wall-related relaxation time of T_1^g = 70 h.

The method of the invention for removing a gas stored in a storage cell 20 of a transport device in accordance with the invention in the vicinity of an external magnetic field, for example the stray field B_{TS} of a nuclear magnetic resonance imaging apparatus, is represented in Figures 7a and b. If the storage cell is to be introduced into the field B_T of the magnetic resonance imaging apparatus, for a medical application for instance, without this involving significant depolarization, the invention proposes, as illustrated in Figure 7a, that the transport device in accordance with the invention be set up with its field B_o parallel to and in the same direction as the external magnetic

field B_{TS}, as shown. The upper part of the transport device facing the magnetic resonance imaging apparatus with the pole shoe 10.1 is then lifted off in the direction indicated by the arrow 302. This makes the storage cell 20 freely accessible. The transport device, designed here in the form of a pot magnet, is shown in its opened state in Figure 7b. As can clearly be seen, the homogenising force is reduced due to the upper section of the pot magnet not being present. Nonetheless, the remaining lower pole shoe 10.2 ensures that the magnetic field lines of the resulting field B_{res} end perpendicular on this pole shoe. This still makes it possible to homogenise the magnetic field B_{res} adequately in the area of the storage cell 20, i.e. to achieve parallel lines of magnetic force, as shown in the drawing. The storage cell can then be removed along arrow 304 in the direction of the symmetrical axis, in the field B_{res} which is still largely homogeneous even with the upper section removed, without a noticeable depolarization of the gas occurring during the brief time taken for removal.

Referring to Figure 8 there is shown, in perspective, a container according to the invention with hexagonal-cylindrical, rather than circular cylindrical symmetry. Container 1 comprises a hexagonal-cylindrical yoke 2 and has separable upper 1.1 and lower 1.2 portions. Magnetic field sources, pole shoes, etc. may be disposed, e.g. as described for the variants described above, if necessary including shims to combat edge effects to field B_o.

The gas contained in the storage cell designed in accordance with the invented method still possesses an adequate degree of polarization for the intended applications after being removed within the strong magnetic field of the nuclear magnetic resonance imaging

apparatus.

This invention thus provides a device which allows the storage and transport of spin polarized gases over long distances and periods, such as is required in particular for an intended use in the field of medicine. In particular, the invention is characterised by its economical construction, simple design, maximum possible useable volume and very low weight, whereby reliable shielding against external stray fields is provided. The invention thus provides, for the first time, a means which makes the commercial use of ^{3}He and ^{129}Xe feasible, in the field of medicine for example.

Regarding future possible uses of ^{3}He and ^{129}Xe in medicine, particular reference is made to the use of polarized ^{3}He and ^{129}Xe in brilliant, high-resolution, three-dimensional nuclear magnetic resonance imaging of the human respiratory system.

Regarding this application, reference is made to the following publications, the disclosed content of which is included in full in this application:

- Bachert et al., Magnetic Resonance in Medicine 36: 192-196 (1996); and

- Ebert et al., THE LANCET 347: 1297-1299 (1996).

In addition, a compact magnet of lightweight construction is presented which provides a magnetic field which is both homogeneous over a wide area, compact, easily transportable and relatively low in cost and which, in particular, also fulfils all requirements in terms of shielding off external magnetic fields which can lead to a depolarization of the nuclear spin. The use of commercially-available small permanent magnets

represents a quite decisive advantage in terms of both construction and economy.

In addition, there is the extremely high permeability and low remanence of the μ-metal which is in this case used for the first time for the construction of very thin, therefore lighter, and yet highly-efficient pole shoes for the homogenisation of the magnetic field.

The low magnetic flux also allows the use of a yoke made of thin soft iron sheet which, at the same time, due to the pot form and the associated possibility of radial conduction, adequately shields off external interference fields.

This means that, in this invention, a magnet with an extremely favourable ratio of homogeneous field volume to total volume and very low weight is made available for the first time.

In a slightly inferior construction form, pole shoes of magnetically soft iron can be used in place of the μ-metal pole shoes which, while reducing the quality of the field, represents a more economical variant in terms of price. It is also possible to replace the permanent magnets with magnetic field coils which fulfil the same function, in order to generate the necessary flux at the points required within the pot magnet.

Finally, a method for removing a spin polarized gas from the pot unit in accordance with the invention is described in which the degree of polarization is also maintained in the presence of external magnetic fields, for example those of a nuclear magnetic resonance imaging apparatus.

Claims:

1. A magnetically shielded container (1) having disposed in parallel opposed position on an axis (S) thereof magnetic field homogenizing pole shoes (10.1, 10.2), having disposed about said pole shoes a magnetically shielding yoke (2), said·pole shoes and yoke enclosing a magnetic chamber (26), said container further comprising magnetic field sources (2.4,2.5) disposed about and radially distanced from said axis whereby there exists within said chamber subsantially homogeneous magnetic field B_o oriented in the direction of said axis and whereby there is a usable volume within said chamber where the ratio of the magnetic field gradient in the direction transverse to said axis to said magnetic field B_o has a value of no more than 1.5×10^{-3}/cm.

2. A container as claimed in claim 1 wherein said ratio has a value of no more than 7×10^{-4}/cm.

3. A container as claimed in either·of claims 1 and 2 wherein the ratio of the volume of said usable volume to the volume of said chamber (26) is greater than 1:30.

4. A container as claimed in either of claims 1 and 2 wherein the ratio of the volume of said usable volume to the volume of said chamber (26) is greater than 1:5.

5. A container as claimed in either of claims 1 and 2 wherein the ratio of the volume of said usable volume to the volume of said chamber (26) is greater than 1:2.

6. A container as claimed in any one of claims 1 to 5 wherein the volume of said usable volume is at least 50 mL.

7. A container as claimed in any one of claims 1 to 5 wherein the volume of said usable volume is at least 100 mL.

8. A container as claimed in any one of claims 1 to 5 wherein the volume of said usable volume is at least 200 to 2000 mL.

9. A container as claimed in any one of claims 1 to 8 wherein said pole shoes (10.1,10.2) are of μ-metal or soft iron.

10. A container as claimed in any one of claims 1 to 9 wherein said yoke (2) is of a material which is not magnetically saturatable at magnetic field strengths below 1 Tesla.

11. A container as claimed in any one of claims 1 to 9 wherein said yoke (2) is of a material which is not magnetically saturatable at magnetic field strengths below 2 Tesla.

12. A container as claimed in any one of claims 1 to 11 wherein said magnetic field sources (2.5) are disposed around the peripheries of each of said pole shoes (10.1, 10.2).

13. A container as claimed in claim 11 wherein said magnetic field sources are disposed between the side wall (2.2) and end walls (2.1.1,2.1.2) of said yoke.

14. A container as claimed in any one of claims 1 to 11 wherein said magnetic field sources (2.4) are disposed about said axis (S) on a plane (4) between said pole shoes (10.1,10.2)

15. A container as claimed in claim 14 wherein said magnetic field sources (2.4) are disposed between two sections (2.3) of said yoke (2).

16. A container as claimed in any one of claims 1 to 11 wherein one array of magnetic field sources (2.5) is disposed around the peripheries of each of said pole shoes (10.1,10.2) and a further array of magnetic field sources (2.5) is disposed about said axis (S) on a plane (4) between said pole shoes (10.1,10.2).

17. A container as claimed in claim 16 wherein said arrays (2.4,2.5) of magnetic field sources are disposed as defined in claims 12 and 14.

18. A container as claimed in any one of claims 1 to 17 further comprising a magnetic screen (40) disposed about said axis (S) within said yoke (2).

19. A container as claimed in any one of claims 1 to 18 further comprising at least one shim disposed about said axis (S) within said yoke (2).

20. A container as claimed in any one of the preceding claims for which the ratio between the total weight of the container (1) and the volume of the magnetic chamber (26) is no more than 1 kg/L.

21. A container as claimed in any one of the preceding claims for which the ratio between the total weight of the container (1) and the volume of the magnetic chamber (26) is no more than 0.2 kg/L.

22. A container as claimed in any one of the preceding claims for which the ratio between the total weight of the container (1) and the volume of the magnetic chamber (26) is no more than 1/30 kg/L.

23. A container as claimed in any one of the preceding claims which is openable and sealingly closable.

24. A container as claimed in any one of the preceding claims wherein said pole shoes (10.1,10.2) are circular and said yoke (2) is substantially cylindrical.

25. A container as claimed in any one of the preceding claims wherein said pole shoes (10.1,10.2) are supported by magnetically resistant elements (16).

26. A container as claimed in claim 25 wherein said elements (16) are of rigid porous plastic.

27. A container as claimed in any one of the preceding claims further comprising a gas storage cell (20) disposed in said usable volume in said magnetic chamber (26).

28. A container as claimed in claim 27 wherein at least the inner walls of said cell are formed of a material essentially free of paramagnetic substances.

29. A container as claimed in claim 28 wherein said material is a very low iron concentration glass.

30. A container as claimed in claim 29 wherein said glass has an iron concentration of less than 20 ppm.

31. A container as claimed in any one of claims 27 to 30 wherein the walls of said cell (20) are uncoated.

32. A container as claimed in any one of claims 27 to 31 wherein the wall of said storage cell (20) is of a low iron content glass, the iron content being sufficiently low that the ratio between the wall-related depolarization relaxation time T_1^w for nuclear spin

polarized ^3He and the volume-to-inner surface area of said cell is at least 10 hours/cm.

33. A container as claimed in any one of claims 27 to 32 wherein said cell (20) is provided with a valve (22) to permit introduction and removal of gas.

34. A container as claimed in any one of claims 27 to 33 wherein said cell (20) contains nuclear spin polarized gas.

35. A container as claimed in claim 34 wherein said gas is ^3He or ^{129}Xe or contains ^{19}F, ^{13}C or ^{31}P.

36. A container as claimed in any one of claims 27 to 35 wherein said cell (20) has an internal volume of at least 50 mL.

37. A container as claimed in any one of claims 27 to 35 wherein said cell (20) has an internal volume of betweem 100 mL and 1 m^3.

38. A container as claimed in any one of the preceding claims in transportable form.

39. A container as claimed in any one of the preceding claims further comprising a magnetic field sensor (32) disposed within said magnetic chamber (26).

40. A container as claimed in claim 39 further comprising means for moving said sensor (32) relative to a gas storage cell (20) disposed in said magnetic chamber (26).

41. A container as claimed in claim 39 further comprising a source (30) for a time variant magnetic field disposed in said magnetic chamber (26).

42. A container as claimed in any one of the preceding claims further comprising a spacer (12,205) so disposed as to maintain said pole shoes (10.1,10.2) in parallel opposed relationship.

43. A container as claimed in any one of the preceding claims having a double-hulled (200.1,200.2) construction whereby said yoke (2) is provided at least in part by the inner hull (200.2).

44. A container as claimed in any one of the preceding claims in the form of a magnetic device (1) with an internal space which provides a high-volume, largely homogeneous, shielded magnetic field within its interior, whereby the magnetic device (1) features homogenising μ-metal plates as pole shoes (10.1, 10.2), wherein a ratio of 1:1.5 can be achieved between the useable volume of the magnetic device within which a homogeneous magnetic field is present and the overall volume of the magnetic device and the homogeneity condition

$$G_r \leq 1.5 \times 10^{-3}/\text{cm}$$

is fulfilled within the useable volume, whereby G_r is the relative transverse magnetic field gradient.

45. A gas storage cell (20) containing a nuclear spin polarized gas in a gas storage space surrounded by a cell wall, the wall being of an uncoated material which on the surface contacting said gas storage space is substantially free of paramagnetic substances.

46. A cell as claimed in claim 45 wherein said wall is of a low iron content glass, the iron content being sufficiently low that the ratio between the wall-related depolarization relaxation time T_1^w for nuclear spin

polarized ^3He and the volume-to-inner surface area of said cell is at least 10 hours/cm.

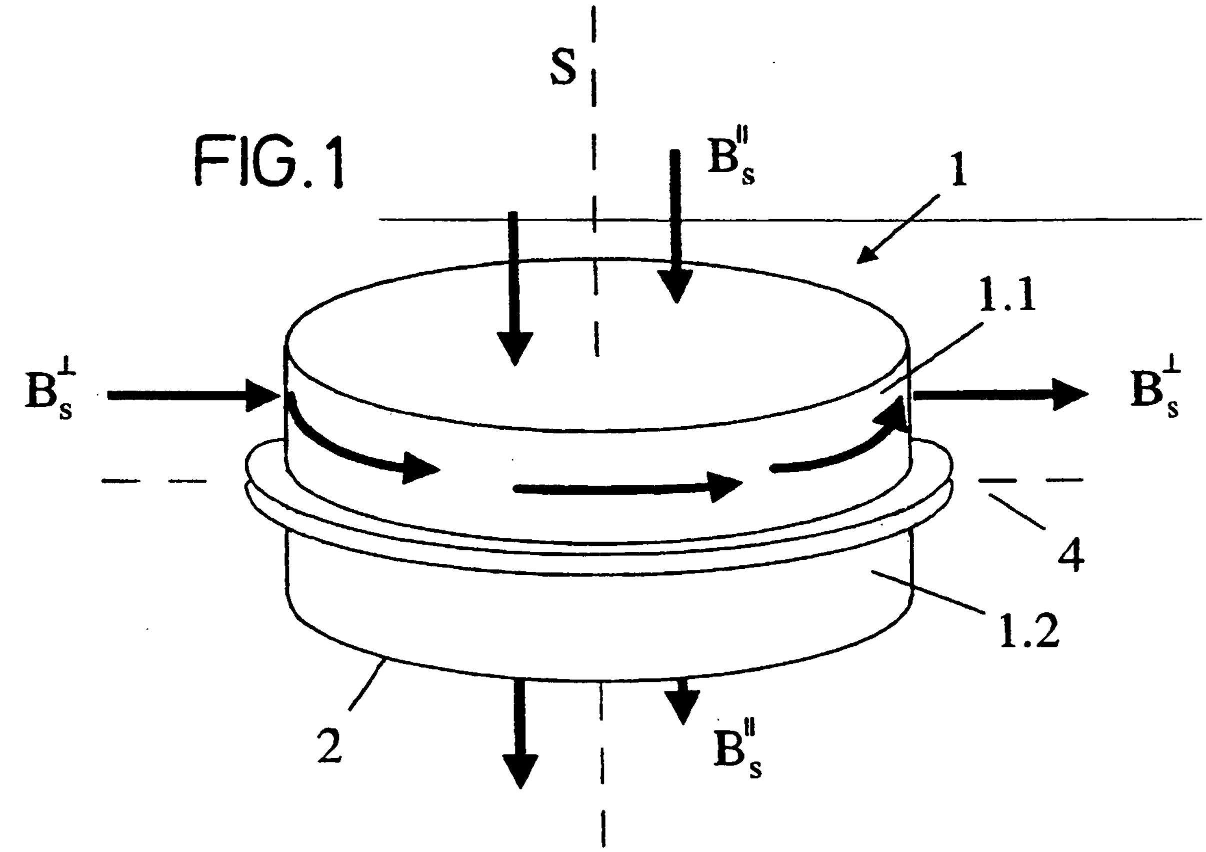
47. A method for the removal of a nuclear spin polarized gas from a gas storage cell (20) in a container as claimed in any one of claims 1 to 38 comprising:

(i) positioning said container with said axis (S) parallel to the field direction of an external substantially homogeneous magnetic field;

(ii) opening said container by removing a portion comprising one of said pole shoes (10.1); and

(iii) removing said cell (20) in the direction of said axis.

FIG. 1


S
$B_s^{\parallel}$
1
1.1
$B_s^{\perp}$
$B_s^{\perp}$
4
1.2
2
$B_s^{\parallel}$

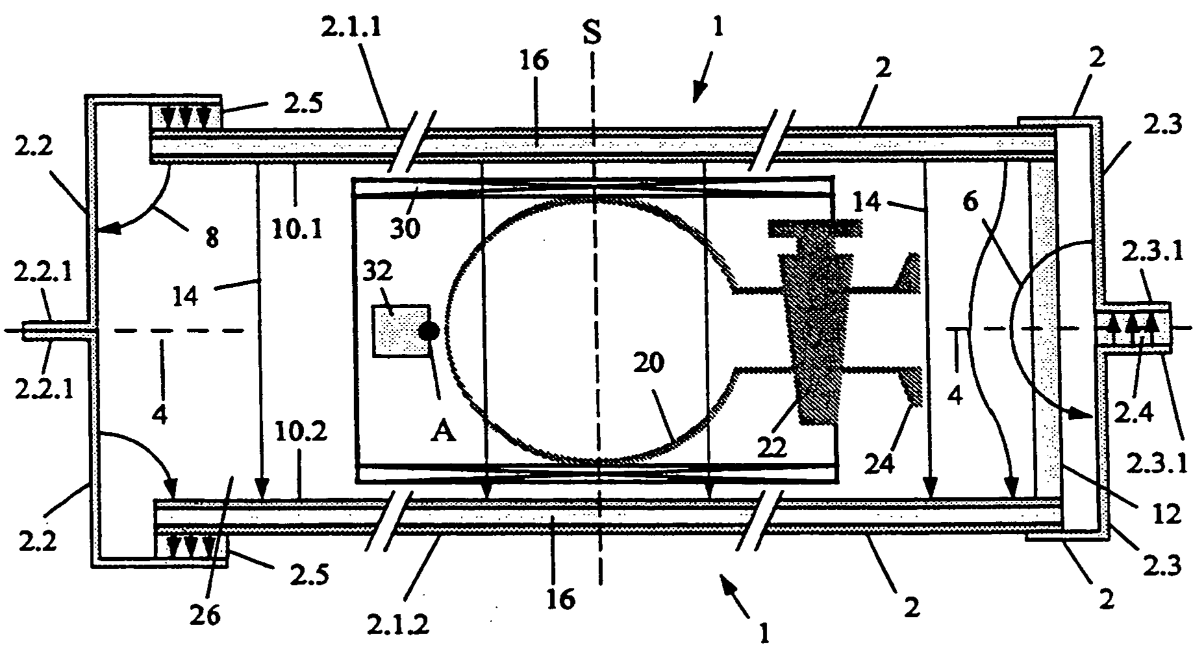

2.1.1
16
S
1
2
2
2.5
2.2
2.3
8
10.1
30
14
6
2.3.1
2.2.1
14
32
2.2.1
4
20
4
2.4
A
22
24
2.3.1
10.2
12
2.2
2.5
26
16
2.1.2
1
2
2
2.3

FIG. 2

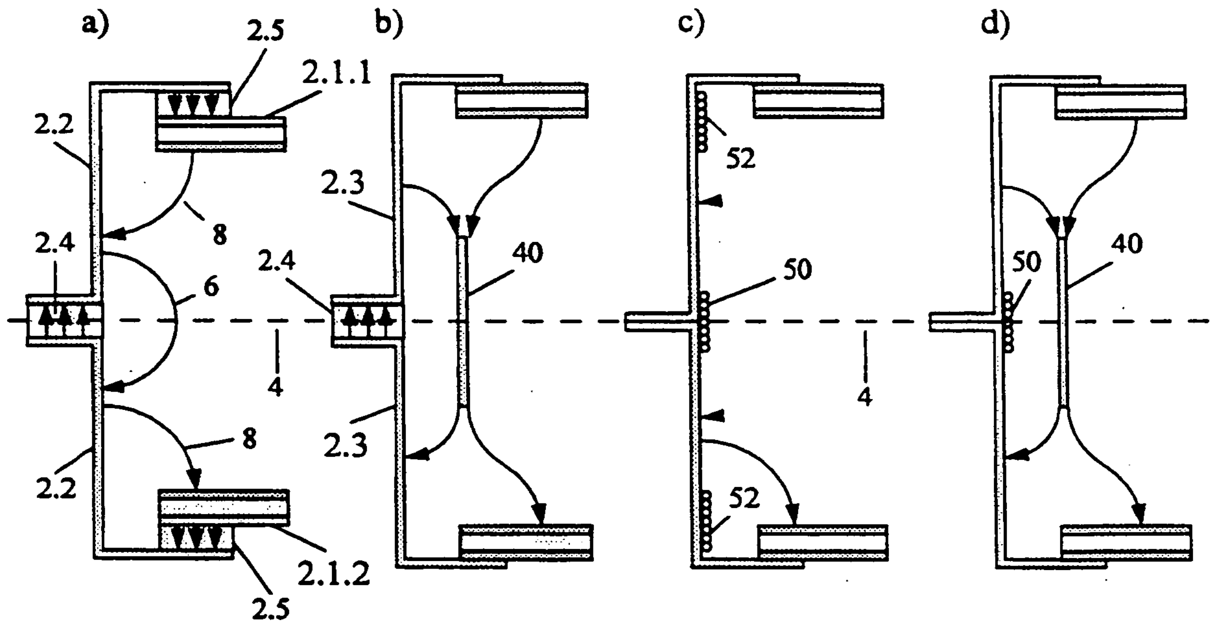

a)
b)
c)
d)
2.5
2.1.1
2.2
52
2.3
8
2.4
40
6
50
2.4
50
40
4
4
8
2.3
2.2
52
2.1.2
2.5

FIG. 3

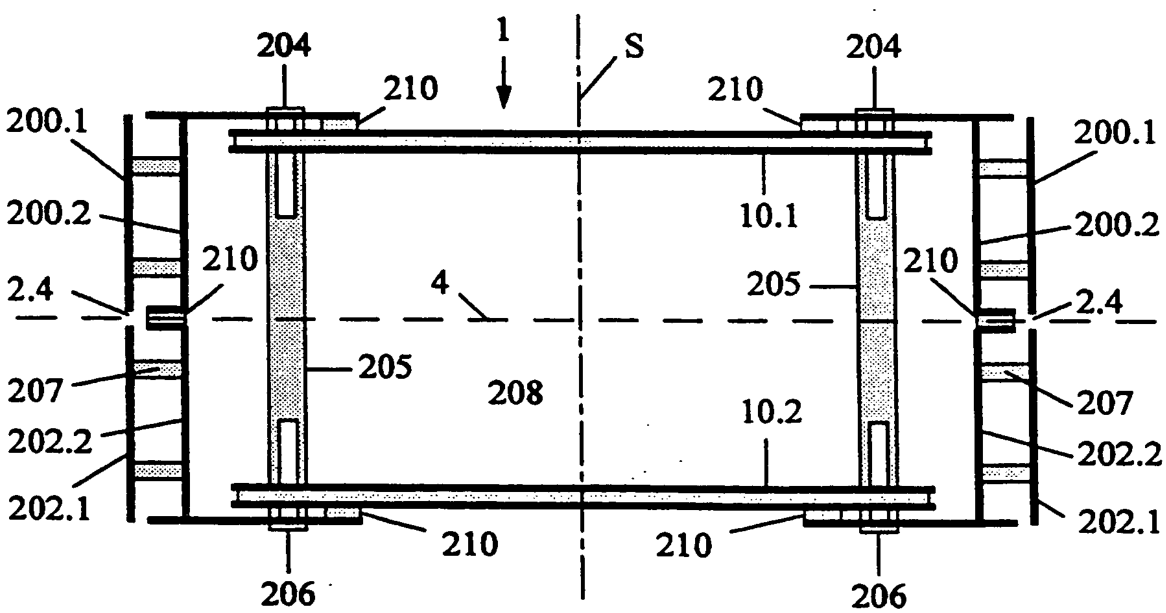

1
S
204
204
210
210
200.1
200.1
10.1
200.2
200.2
210
210
2.4
4
205
2.4
205
207
208
207
10.2
202.2
202.2
202.1
202.1
210
210
206
206

FIG. 4

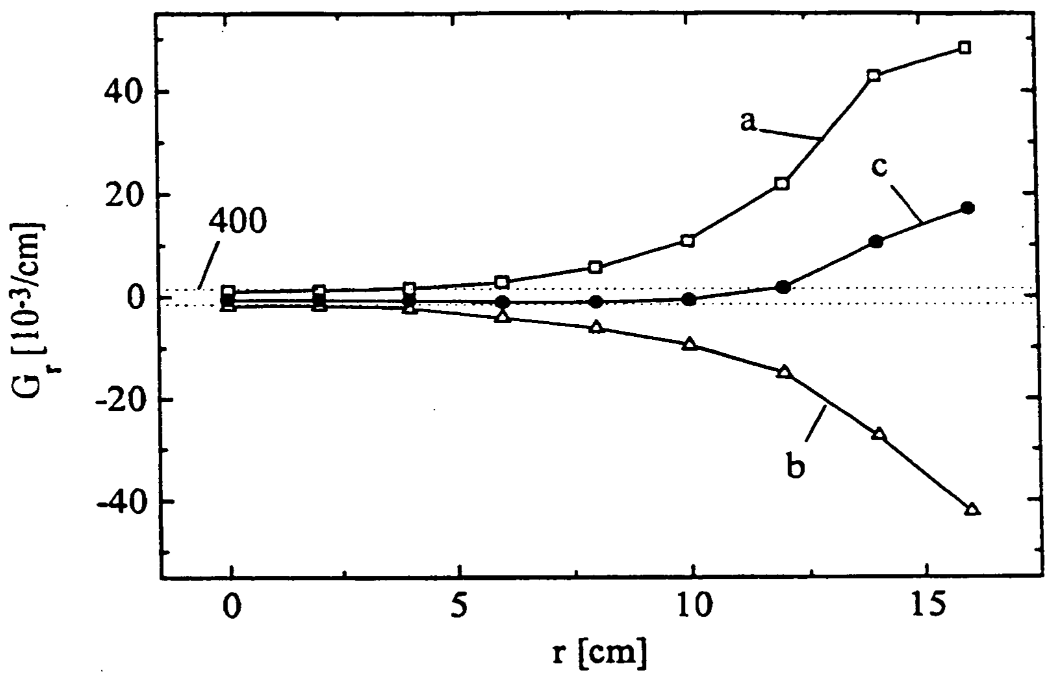

40
20
0
-20
-40
400
a
b
c
G_r [10^{-3}/cm]
0
5
10
15
r [cm]

FIG. 5A

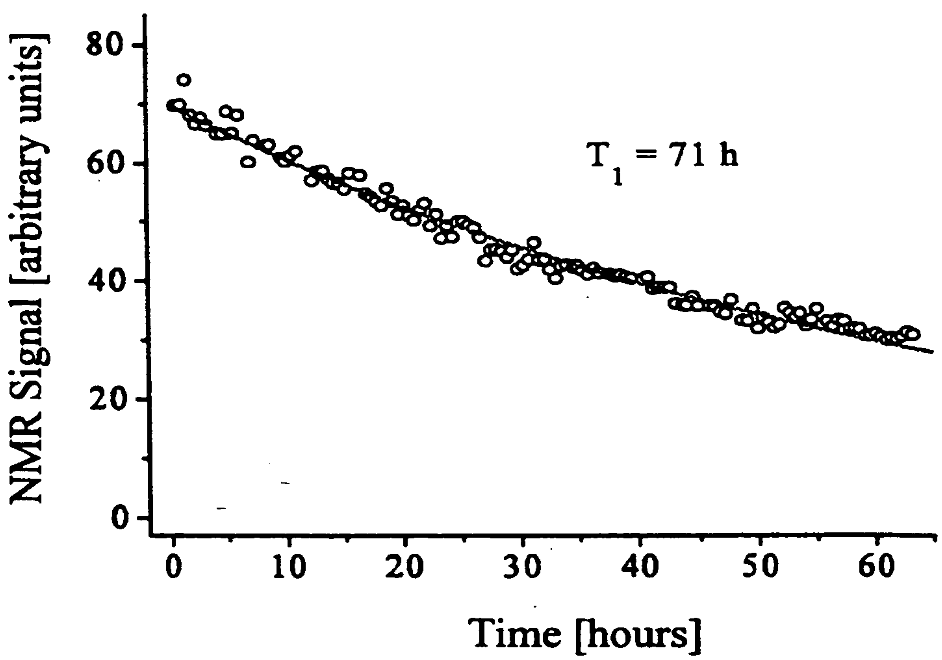

80
60
40
20
0
NMR Signal [arbitrary units]
T_1 = 71 h
0
10
20
30
40
50
60
Time [hours]

FIG. 6

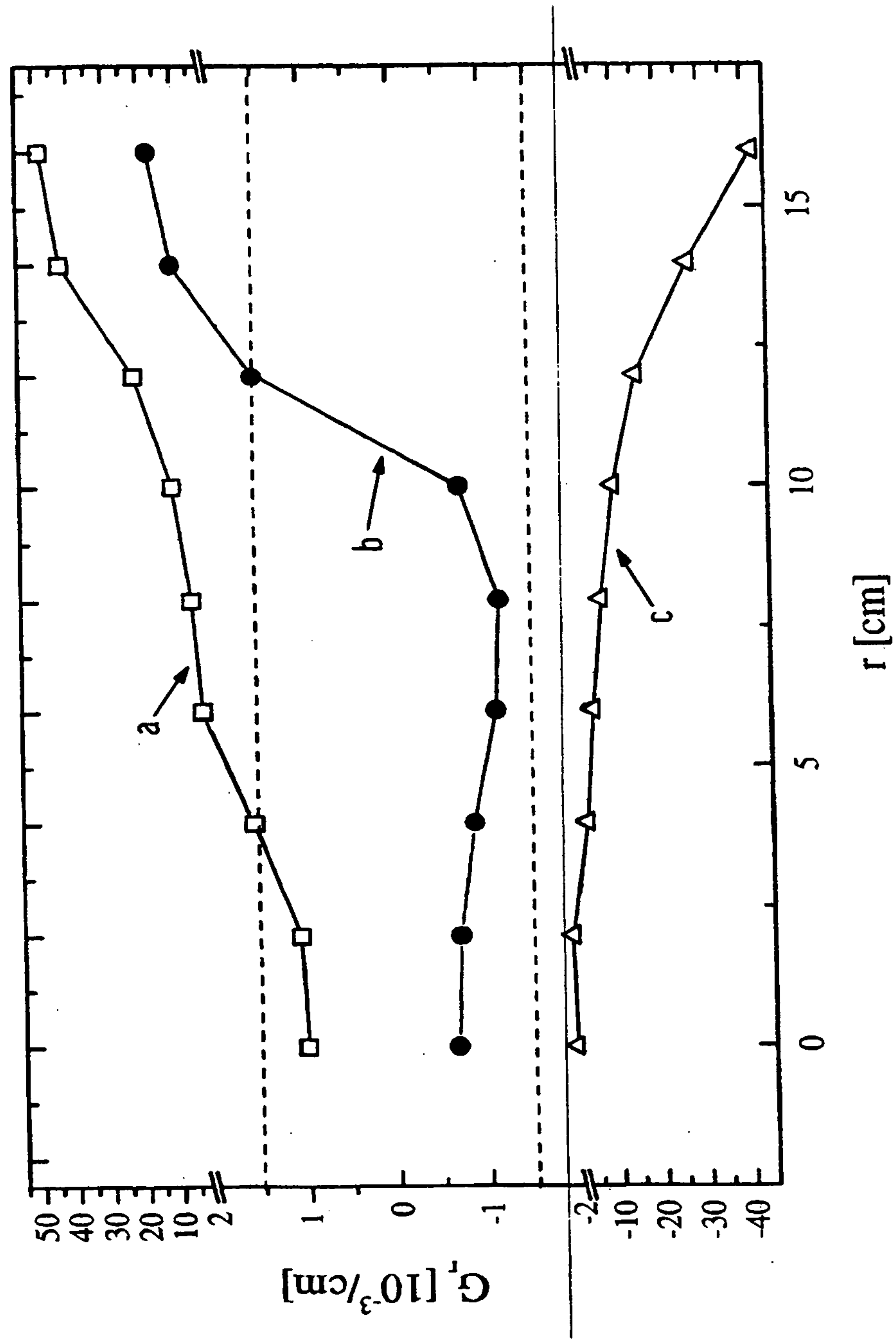


FIG. 5B

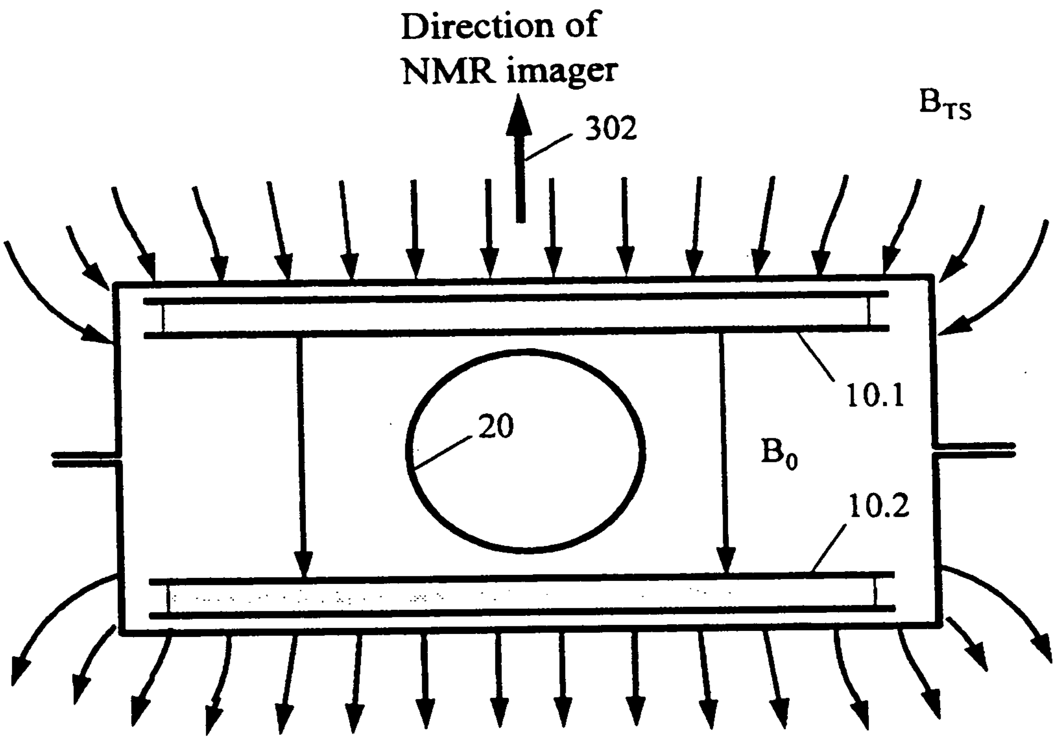

Direction of
NMR imager
302
B_{TS}
10.1
20
B_0
10.2

FIG. 7A

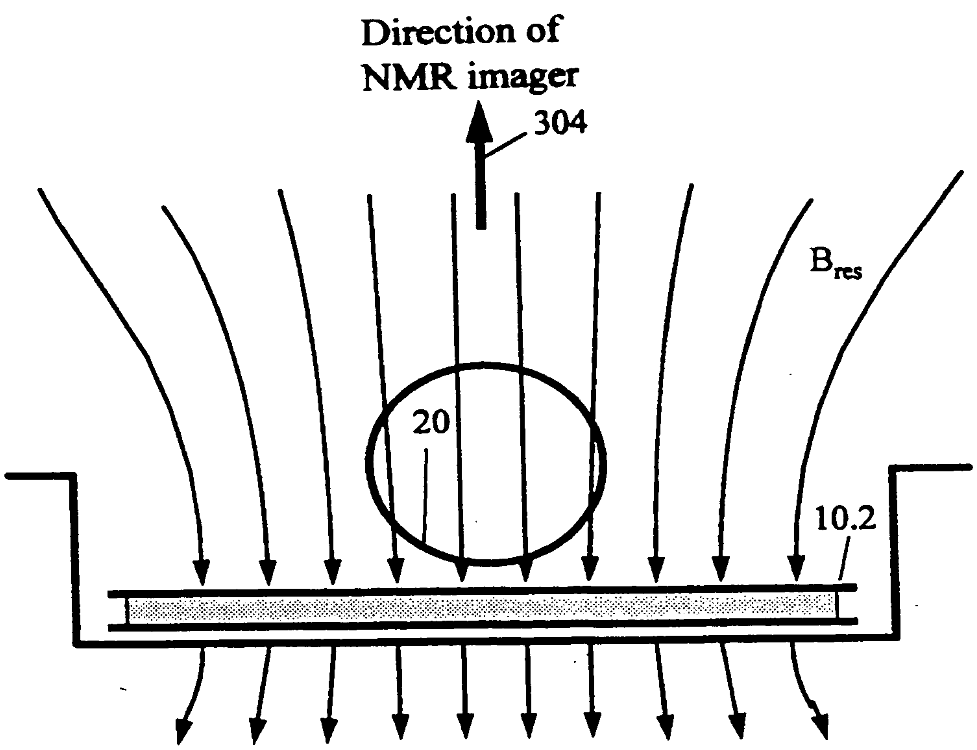

Direction of
NMR imager
304
B_{res}
20
10.2

FIG. 7B

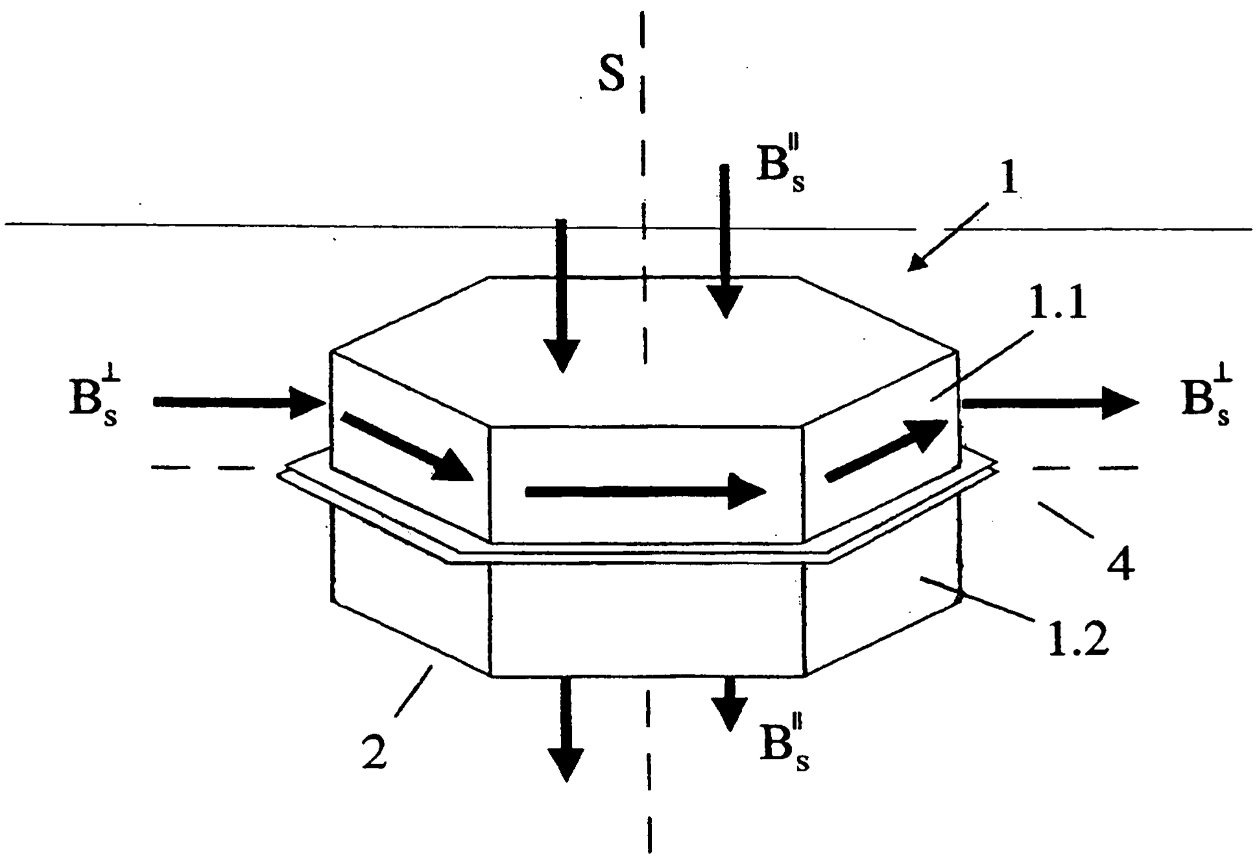


FIG. 8

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/06056

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G21F5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G21F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 800 158 A (GROSBARD G) 26 March 1974 see claims 1-12; figures 1,9,19 ---	1-9,16, 20-23, 38,45
A	EP 0 540 392 A (THOMSON TUBES ELECTRONIQUES) 5 May 1993 see claims 1-3,5,6; figures 1-3 ---	1-8,18, 20-23, 25-28, 33-38,45
A	US 5 043 529 A (VANESKY FRANK W ET AL) 27 August 1991 see claims 1,5,6,10-14; figures 1-3 -----	1-8,18, 23,39, 40,43,45

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 January 1999	13/01/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Deroubaix, P

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 98/06056

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
US 3800158	A	26-03-1974	NONE			
EP 0540392	A	05-05-1993	FR	2683387	A	07-05-1993
			DE	69202437	D	14-06-1995
			DE	69202437	T	14-09-1995
			JP	6028989	A	04-02-1994
			US	5304792	A	19-04-1994
US 5043529	A	27-08-1991	EP	0467179	A	22-01-1992
			JP	4297227	A	21-10-1992